

## Is Obesity a Risk Factor for Menstrual Abnormality in Saudi Females?

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### Abstract

**Objective:** To estimate the risk of obesity as a cause of abnormal menstruation among Saudi females.

**Setting:** King Abdulaziz Medical City, National Guard hospital, Obstetrics and Gynaecology Department, Gynecologic clinics, Riyadh, Saudi Arabia.

**Design:** A retrospective case-control study.

**Population:** A cohort of 145 females, 72 with normal menstruation, and 73 with abnormal menstruation.

**Methods:** The data were collected from patients charts: Age, abnormality of menstrual type, weight (kg), BMI (kg/m<sup>2</sup>), and waist circumference (wc), blood samples were obtained: fasting Insulin, glucose level, total testosterone, TSH, cholesterol, HDL, and LDL. With inclusion criteria: 1) age between 11 to 35 years, and 2) married, and exclusion criteria: 1) No hormonal treatment, 2) not pregnant, 3) not breast feeding, and 4) not diabetic patient.

**Results:** The results of unadjusted analyses show that abnormal menstruation was more common among obese women (OR = 5.5; 95% CI: 2.156-14.232), women with medium central obesity (OR = 5.5; 95% CI: 1.998-15.329), and high central obesity (OR = 9.4; 95% CI: 3.548-24.695) compared with their reference. High TSH, high Testosterone, high Cholesterol, high insulin, low HDL, and high LDL were associated with abnormal menstruation (p-values < 0.05). The adjusted odds of abnormal menstruation increased with increasing central obesity, (OR = 10.4; 95% CI: 2.927-36.946) with medium and (OR = 16.0; 95% CI: 4.476-57.475) with high central obesity.

**Conclusion:** An increased risk for abnormal menstruation is influenced by central obesity, heavy weight, and hormone imbalance.

**Keywords:** Abnormal menstruation; Central obesity; Body mass index

**Abbreviations:** LDL: Low-Density-Lipoprotein; VLDL: Very-Low-Density-Lipoprotein; HDL: High-Density-Lipoprotein; CHD: Coronary Heart Disease

### Introduction

Obesity has become one of the most important public health problems in Saudi Arabia the prevalence of overweight (BMI = 26-29.9 kg/m<sup>2</sup>) was 36.9%, in the female 31.8%, and obesity (BMI ≥ 30 kg/m<sup>2</sup>) was 35.5%, in the female 44%, while morbid obesity (severe = gross = BMI ≥ 40 kg/m<sup>2</sup>) 3.2% [1]. As the prevalence of obesity increases, the prevalence of the co-morbidities associated with obesity have been increased [2]. The endocrine and metabolic disorders: Impaired glucose tolerance [3], insulin resistance [4], diabetes mellitus type 2 [5-30]. The Insulin resistance with hyperinsulinemia found to be characteristic of obesity, and even is present before the onset of

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hyperglycemia. After the onset of obesity, the first demonstrable changes are impairment in glucose metabolism, and increased insulin resistance, which results in hyperinsulinemia. The hyperinsulinemia in turn increases hepatic plasminogen activator inhibitor-1 synthesis and sodium reabsorption. These changes contribute to hyperlipidemia and hypertension in obese persons.

The insulin resistance characteristic of type 2 diabetes results from a combination of obesity, and genetic factors. In a study of non-diabetic offspring of two parents with type 2 diabetes, insulin sensitivity was similar to that of normal persons with no first-degree relatives with type 2 diabetes at near ideal body weight [30]. Obesity is associated with several deleterious changes in lipid metabolism.

Central fat distribution plays an important role in the serum lipid abnormalities, also unfavourable obesity-related effects include high serum concentrations of cholesterol, low-density-lipoprotein (LDL) cholesterol, very-low-density-lipoprotein (VLDL) cholesterol, triglycerides, and reduction in serum high-density-lipoprotein (HDL) cholesterol of about 5 percent [31]. The last effect may be most important since a low serum HDL cholesterol concentration carries a greater relative risk of coronary heart disease (CHD) than hypertriglyceridemia. The cardiovascular diseases such as atherosclerosis, dyslipidemia and hypertension are common [10-12].

Hyperandrogenism and early onset of polycystic ovarian syndrome, with irregular menstruation, is associated with obesity in most of the cases, Obesity plays a role in acceleration of growth and bone age leading to early onset of sexual maturation in girls [6-9].

Cholelithiasis and Fatty liver disease, found to be resolved with weight loss [13-16]. Pulmonary co-morbidities of obesity include obstructive sleep apnea, hypoventilation syndrome during sleep and episodes of severe oxygen desaturation, which resolve after weight loss as well [17-19]. Neurologic idiopathic intracranial hypertension, Slipped capital femoral epiphysis, and Tibia vara are common complications. Acne, hirsutism, acanthosis nigricans, striae, candidal intertrigo and skin abscesses are the common dermatological complications. Obesity can be cause of psychosocial consequences (Alienation, poor self esteem and depression) [20-25].

Obesity refers to an excess of body fat. The body mass index (BMI) is the accepted standard measure of obesity. Body mass index provides a guideline for weight in relation to height, and is equal to the body weight divided by the height squared [26]. The (BMI) between 26-29, 9 are considered overweight; those with BMI  $\geq 30$  are considered to be obese, while severe is  $\geq 40$ . The incidence of obesity in adolescent in United States is 18.1%, and severe is 12.5% [27]. Obese women had at least a twofold greater odd of having an irregular cycle compared with those of normal weight [28]. Fasting glucose, insulin, and testosterone are positively associated with obesity [29]. Weight loss and exercises are the main management of this disorder. No study had been done in Saudi Arabia examining the risk of obesity in menstrual abnormality among Saudi females. The aim of this study is to assess the associations between the obesity and abnormal menstruation among Saudi females.

### Methods and Materials

This study was a case-control study, total of 145 Saudi females: n = 72 with normal menstruation, and n = 73 with abnormal menstruation who received gynecological care in the clinic within two years (2011-2013), at King Abdulaziz Medical City in Riyadh, Saudi Arabia (KAMC-R). An eligibility criterion was women who are married with age between 11 to 35 years. Exclusion criteria were: 1) not on hormonal treatment, 2) not pregnant, 3) not breast feeding, and 4) not diabetic patient. The data were collected from charts obtaining the age, the menstrual type (normal, abnormal), the weight (kg), BMI (kg/m<sup>2</sup>) which categorized into three groups: normal  $\leq 25$ , overweight (26-29.9), obese ( $\geq 30$ ), waist circumference (wc): normal < 80 cm, overweight 80-88 cm, and > 89 cm for central obesity using a non-stretch paper measuring tape at narrowest point between the costal border and the iliac crest. Blood samples were obtained to measure fasting insulin level, glucose level, total testosterone, TSH, cholesterol, HDL, and LDL.

### Statistical analysis

The sample size was calculated with odds of 3.0, total of n = 145 women, n = 72 with normal menstruation, and n = 73 with abnormal menstruation.

Chi-square tests (Univariate analyses) were used to investigate whether demographic; obesity, increased central obesity, or hormones measurements were related to abnormal menstruation. Multivariate stepwise logistic regression was employed to identify the important risk factors that associated with an increased risk of abnormal menstruation. P-value  $\leq 0.05$  was considered to be statistically significant. We used odds ratios with 95% confidence intervals to estimate the strength of associations. The data were analyzed with SAS, V 9.2 (SAS Institute Inc., SAS Campus Drive, Cary, North Carolina 27513, USA).

**Results**

Table 1 shows the sample characteristics of the examined women. Of the 145 women, 30 (20.7%) were normal weight, 21 (14.5%) were overweight, and 94 (64.8%) were obese (Figure 1). The mean age of women was 24.1 ( $\pm$  SD = 3.41) years with a weight of 80.28 ( $\pm$  SD = 16.71) kg. 44% of the participant women had high waist circumference (> 89 cm), 29% had waist circumference between 80-88 cm, and 26.9% had normal waist circumference. Overall, 23.4% had high testosterone levels, 29.7% had high cholesterol levels, 11% had high insulin levels, 64.8% had low HDL levels, and 69.7% had high LDL levels.

Characteristics		Overall Sample N=145	
		n	%
BMI	Normal	30	20.7
	Overweight	21	14.5
	Obese	94	64.8
Waist circumference	< 80 cm	39	26.9
	80-88cm	42	29.0
	> 89 cm	64	44.1
Fasting Glucose	High	1	0.7
	Normal	144	99.3
TSH	High	7	4.8
	Normal	138	95.2
Testosterone	High	34	23.4
	Normal	111	76.6
cholesterol	High	43	29.7
	Normal	102	70.3
Insulin	High	16	11.0
	Normal	129	89.0
HDL	Low	94	64.8
	Normal	51	35.2
LDL	High	101	69.7
	Normal	44	30.3
Menstruation	Abnormal	73	50.3
	Normal	72	49.7
Age	Range = 18-34 yrs	24.1 $\pm$ 3.41	
Weight	Range = 52-137 kg	80.28 $\pm$ 16.71	

**Table 1:** Saudi females demographic and clinical characteristics.

Patients' demographic and clinical characteristics stratified by menstruation types are shown in Table 2. The results of unadjusted (univariate) analyses show that there was significant association between obesity and menstrual abnormalities (80.8% among abnormal menstruation group vs. 48.6% among normal menstruation group, p-value = 0.001).

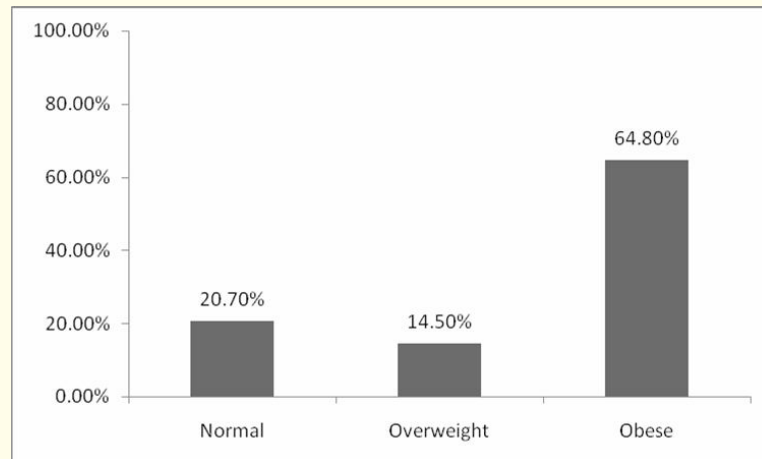


Figure 1: Obesity among Saudi females.

Figure 2 shows the percents of obesity among normal and abnormal menstruation groups. We also observed low frequency of the normal weight in the case group 7 (9.6%) while in the control group this value was 23 (31.9%). Obese women had 5.5 greater odds of having menstruation abnormalities compared with those of normal weight (OR = 5.5; 95% CI = 2.156-14.232). High (> 89 cm) central obesity was associated with menstruation abnormalities (58.9% of abnormal menstruation group vs. 29.2% of normal menstruation group, p-value = 0.001). Women with high (OR = 9.4; 95% CI = 3.548-24.695) or medium (OR = 5.5; 95% CI = 1.998-15.329) central obesity were more likely to have an abnormal menstruation compared with normal waist circumference.

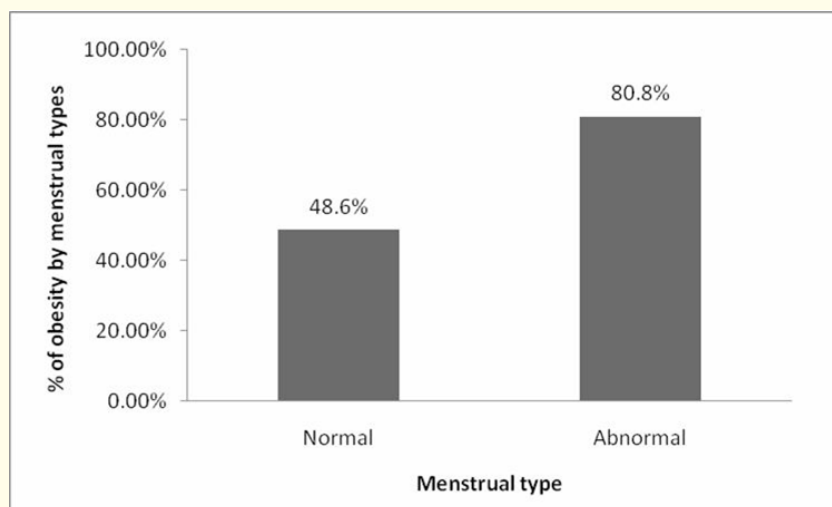


Figure 2: Association of obesity with irregular menstruation.

Characteristics		Abnormal		Normal		P-value	OR(95 CI)
		73(50.3%)		72(49.7%)			
		n	%	n	%		
BMI	Normal	7	9.6	23	31.9	0.001*	1.0
	Overweight	7	9.6	14	19.4		1.6(0.475-5.680)
	Obese	59	80.8	35	48.6		5.5(2.156-14.232)
Waist circumference	< 80 cm	7	9.6	32	44.4	0.001*	1.0
	80-88 cm	23	31.5	19	26.4		5.5(1.998-15.329)
	> 89 cm	43	58.9	21	29.2		9.4(3.548-24.695)
Fasting Glucose	Normal	72	98.6	72	100	1.000	1.0
	High	1	1.4	0	0.0		2.0(0.1699-2.355)
TSH	Normal	66	90.4	72	100	0.013*	1.0
	High	7	9.6	0	0.0		2.1(1.757-2.489)
Testosterone	Normal	49	67.1	62	86.1	0.007*	1.0
	High	24	32.9	10	13.9		3.0(1.328-6.946)
Cholesterol	Normal	43	58.9	59	81.9	0.002*	1.0
	High	30	41.1	13	18.1		3.2(1.480-6.772)
Insulin	Normal	58	79.5	71	98.6	0.001*	1.0
	High	15	20.5	1	1.4		18.4(2.355-143.171)
HDL	Normal	19	26.0	32	44.4	0.020*	1.0
	Low	54	74.0	40	55.6		2.3(1.130-4.577)
LDL	Normal	10	13.7	34	47.2	0.001*	1.0
	High	63	86.3	38	52.8		5.6(2.503-12.695)
Age/years	18-34	23.5 ± 3.3		24.6 ± 3.5		0.052	0.9(0.822-1.002)
Weight/kg	52-137	87.3 ± 15.6		73.2 ± 14.7		0.001#	1.1(1.036-1.091)

**Table 2:** Characteristics of menstruation abnormalities compared with the normal group. \*The Chi-square statistic/Fisher's exact test is significant at  $\alpha = 0.05$ .

#Independent t test is significant at  $\alpha = 0.05$ .

Obesity and high central obesity are associated with increased risks of abnormal menstruation (Figure 3 and 4). Abnormal menstruation was significantly associated with higher level of TSH (p-value = 0.013), higher level of testosterone (p-value = 0.007), higher level of cholesterol (p-value = 0.002), higher level of insulin (p-value = 0.001), lower level of HDL (p-value = 0.020), and higher level of LDL (p-value = 0.001). The results of independent t-test analysis, indicate that there was significant difference in the body weight of females (kg) between the two groups (87.3 ± 15.6 among abnormal menstrual group vs. 73.2 ± 14.7 among normal menstrual group, p-value = 0.001). There was no significant difference in the age of two groups (p-value = 0.052). There was no difference in fasting glucose frequency between abnormal and normal menstruation groups (p-value = 1.000).

The findings of multivariate stepwise logistic regression after controlling for all risk factors are shown in Table 3. In the multivariate analysis, a higher level of testosterone was positively associated with abnormal menstruation (p-value = 0.001; OR = 7.6; 95% CI: 2.323-24.561). A higher level of insulin was also positively associated with abnormal menstruation (p-value = 0.026; OR = 10.9; 95% CI: 1.330-88.507). As was the case for univariate analyses, high (p-value = 0.001; OR = 16.0; 95% CI: 4.476-57.475) and medium (p-value = 0.034; OR = 10.4; 95% CI: 2.927-36.946) central obesity were associated with an increased risk of abnormal menstruation.

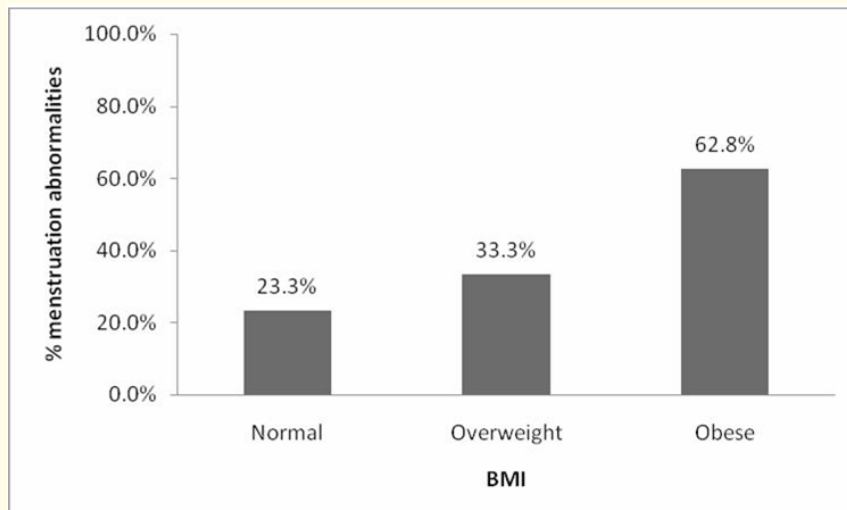


Figure 3: Association of BMI (kg/m<sup>2</sup>) with menstruation abnormalities.

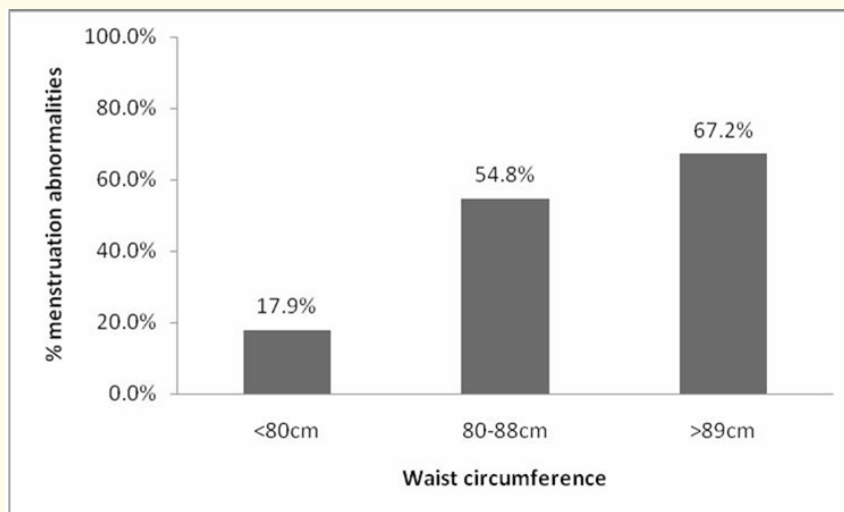


Figure 4: Association of waist circumference (cm) with menstruation abnormalities.

### Discussion

The present study was conducted to assess the risk of obesity as a cause of abnormal menstruation among Saudi females, and its effect on the levels of fasting glucose, Insulin, Testosterone, TSH (thyroid stimulation hormone), cholesterol, HDL (high density lipoprotein), and LDL (low density lipoprotein), and to estimate the odds of obesity in women with abnormal menstruation as compared to those with normal menstruation. We got 145 women, all were matched in marital and socioeconomic status, and the study age group was ranging between 18-34 years. We found 64.8% of them were obese (BMI > 30), and 44.1% overweight (BMI 26-29.9), whereas 20.7% only were in normal weight (BMI ≤ 25), 44.1% centrally obese waist circumference > 89 cm, and 29.0% centrally overweight,

whereas the normal measurements < 80 cm was 26.9% of total study groups, the average weight was 87.3 ± 15.6 kg in abnormal menstruation group (n = 73), and 73.2 ± 14.7 kg in normal menstruation group (n = 72). This reflects the prevalence of obesity and central obesity among Saudi females.

Parameter	Reference	Estimate	SE	Wald	P- value	OR	95% CI	
Intercept		1.32	0.56	5.53	0.019			
Waist circumference: 80-88	< 80 cm	0.64	0.30	4.48	0.034*	10.4	2.927	36.946
Waist circumference: > 89	< 80 cm	1.07	0.30	12.40	0.001*	16.0	4.476	57.475
Testosterone: High	Normal	1.01	0.30	11.29	0.001*	7.6	2.323	24.561
Insulin: High	Normal	1.19	0.54	4.96	0.026*	10.9	1.330	88.507

**Table 3:** Risk factors associated with irregular menstruation using stepwise logistic regression.

\*The Wald Chi-square statistic is significant at  $\alpha = 0.05$ .

whereas 20.7% only were in normal weight (BMI ≤ 25), 44.1% centrally obese waist circumference > 89 cm, and 29.0% centrally overweight, whereas the normal measurements < 80 cm was 26.9% of total study groups, the average weight was 87.3 ± 15.6 kg in abnormal menstruation group (n = 73), and 73.2 ± 14.7 kg in normal menstruation group (n = 72). This reflects the prevalence of obesity and central obesity among Saudi females.

There were 80.8% obese women with abnormal menstruation, whereas 48.6% were obese in normal menstruation group, by 5.5 times increasing risk (OR) to have abnormal menstruation among obese women (P-value = 0.001) strongly significant. 9.6% normal BMI, but having abnormal menstruation vs 31.9% with normal menstruation. Even more strongly significant relation were found among abnormal menstruation women who were 58.9% of centrally obese group (WC > 89 cm), compare with 29.2% central obesity but with normal menstruation, by increase risk 9.4 times (OR). In normal waist circumference group (WC > 80 cm); we found 9.6% having abnormal menstruation, vs 44.4% with normal menstruation (P-value = 0.001), and 31.5% among group of centrally overweight (WC 80-88 cm) with abnormal menstruation vs 26.4% with normal menstruation, 5.5 times (OR) increase risk of abnormal menstruation (P-value = 0.001),

In regard of hormonal effects, the strength of significant association between the high fasting blood level of Testosterone 32.9% vs 13.9% by increasing risk 3.0 times in abnormal menstruation group (P-value = 0.007), and Insulin 20.5% vs 1.4 % by increasing risk (OR) 18.4 times (P-value = 0.001) were found, but less significant association in elevated TSH 9.6% vs 0.0%, with increasing risk of 2.1 times in abnormal menstruation (P-value = 0.013).

When we looked to the effect on metabolic abnormal values which were in our study Cholesterol, HDL, and LDL; similar strong association found between their abnormal levels and abnormal menstruation, for high Cholesterol 41.1% vs 18.1% normal; OR = 3.2, (P-v = 0.002), low level of HDL (normally should be high due to its protective vascular effect) 74.0% vs 55.6% normal; OR = 2, and (P-v = 0.020), as well elevated level of LDL (badly vascular effect) 86.3% vs 52.8% normal; OR = 5.6, (P-v = 0.001).

In comparison of multivariate risk factors: obesity, and abnormal menstruation and the study variables associated risk; we found the stronger association was the waist circumference > 89 cm which is central obesity; by OR = 16.0, (P-v = 0.001), and elevated level of Testosterone OR = 7.6, (P-v = 0.001), then the waist circumference 80-88 cm centrally overweight by OR = 10.4, (P-v = 0.034), and high Insulin level with OR = 10.9, (P-v = 0.026). The result of our study was matching the results of international researches [31].

**Conclusion**

An increased risk of abnormal menstruation is influenced by increased BMI, central obesity, and associated with hormonal disturbances.

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